PTO/SB/08A/B 08-03) through 07/31/2006. OMB 0651-0031 U.S. DEPARTMENT OF COMMERCE Patent and Trademark C

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

| Substitute for form 1449 PTO |                        |                 |         | Complete If Known      |                             |  |
|------------------------------|------------------------|-----------------|---------|------------------------|-----------------------------|--|
|                              |                        |                 |         | Application Number     | 10/511,009                  |  |
| INFO                         | RMATIC                 | N DISCI         | LOSURE  | Filing Date            | October 12, 2004            |  |
| STAT                         | STATEMENT BY APPLICANT |                 |         | First Named Inventor   | Ronit Satchi-Fainaro et al. |  |
|                              |                        |                 |         | Art Unit               | To be assigned              |  |
| • •                          | (use as many s         | sheets as neces | sary) · | Examiner Name          | To be assigned              |  |
| Sheet                        | 1                      | of              | 6       | Attorney Docket Number | 701039-52585                |  |

|                       |             |  | U.S. PATEN                  | T DOCUMENTS  |  |
|-----------------------|-------------|--|-----------------------------|--|--|
| Examiner<br>initiats* | Cite<br>No. | Document Number Number – Kind Code <sup>2</sup> (il known) | Publication Date MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines Where<br>Relevant Passages or Relevant<br>Figures Appear |
| AR                    | A1          | US 5,164,410   | 11/17/1992                  | Kishimoto et al.                                   |  |
| VB                    | A2          | US 5,166,172   | 11/24/1992                  | Kishimoto et al.                                   | ·  |
| VB                    | A3          | US 5,180,735   | 01/19/1993                  | Kishimoto et al.                                   |  |
| VB                    | -A4         | US 5,180,738   | 01/19/1993                  | Kishimoto et al.                                   |  |
| VB                    | A5          | US 5,290,807   | 03/01/1994                  | Folkman et al.                                     | -  |
| VB                    | A6          | US 5,698,586   | 12/16/1997                  | Kishimoto et al.                                   |  |
| VB                    | A7          | US 6,017,954   | 01/25/2000                  | Folkman et al.                                     |  |
| VB .                  | A8          | US 6,022,888   | 02/08/2000                  | Morishige et al.                                   |  |
| VB                    | A9          | US 6,225,478   | 05/01/2001                  | Morishige et al.                                   |  |
|                       |             |  |                             |  |  |
|                       |             | ·  | <u> </u>                    | <u> </u>   |  |
|                       |             | ·  |                             |  | ·  |
|                       |             |  |                             |  |  |
|                       |             |  |                             |  |  |
|                       |             |  |                             |  |  |
|                       |             |  |                             | ·  |  |
|                       | - 1         |  |                             |  |  |

|           | FOREIGN PATENT DOCUMENTS                            |                         |                  |                             |   |          |  |
|-----------|---|-------------------------|------------------|-----------------------------|---|----------|--|
| Examiner  | Cite  | Foreign Patent Document | Publication Date | Name of Patentee or         | Pages, Columns, Lines                                 | Т        |  |
| fnitials* | No.1 Country Code3 - Number4 - Kind Code5 (# known) |                         | MM-DD-YYYY       | Applicant Of Cited Document | Where Relevant Passages<br>or Relevant Figures Appear |          |  |
| VB        | B1  | WO 01/97776             | 12/27/2001       | Ishihara et al.             | English Abstract                                      | $\top$   |  |
|           | •   |                         |                  |                             |   | Т        |  |
|           |   |                         |                  |                             | :.  | T        |  |
|           |   |                         |                  |                             |   | Т        |  |
|           |   |                         |                  |                             |   |          |  |
|           |   |                         |                  |                             |   |          |  |
|           |   |                         |                  |                             |   | $\vdash$ |  |
|           |   |                         |                  |                             | 1.  | †        |  |

| Examiner<br>Signature | /Venkataraman BalasubramanianQate | 10/02/2006 |
|-----------------------|-----------------------------------|------------|
| Oignatore             | Considered                        | 1          |

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04 ¹ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is
This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2. \*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance

PTO/SB/08A/B 08-03) h through 07/31/2006. OMB 0651-0031 U.S. DEPARTMENT OF COMMERCE it displays a valid OMB control number. Patent and Trademark Under the Paperwork Reduction Act of 199 persons are required to respond to a collection of information uni

| Substitute for form 1449 PTO      | Complete if Known      |                             |  |
|-----------------------------------|------------------------|-----------------------------|--|
|                                   | Application Number     | 10/511,009                  |  |
| INFORMATION DISCLOSURE            | Filing Date            | October 12, 2004            |  |
| STATEMENT BY APPLICANT            | First Named Inventor   | Ronit Satchi-Fainaro et al. |  |
|                                   | Art Unit               | To be assigned              |  |
| (use as many sheets as necessary) | Examiner Name          | To be assigned              |  |
| Sheet 2 of 6                      | Attorney Docket Number | 701039-52585                |  |

|   |                          | NON PATENT LITERATURE DOCUMENTS   | <del>-</del>   |
|---|--------------------------|---|----------------|
| Include name of the author (In CAPITAL LETTERS), title of the article (when appropriate), title of item (book, magazine, journal, senal, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published |                          | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s).                   | L <sub>5</sub> |
| VB  | C1                       | Folkman, J., Angiogenesis. in <i>Harrison's Textbook of Internal Medicine</i> (eds. Braunwald, E. et al.) 517-530 (McGraw Hill, New York, 2001).  |                |
| VB  |                          |   |                |
| VB  | _C3                      | Volpert, O.V. et al., Id1 regulates angiogenesis through transcriptional repression of thrombospondin-1, Cancer Cell, 2:473-483 (2002).   |                |
| VB  | C4                       | Folkman, J., Tumor angiogenesis, Cancer Medicine (eds. Holland, J. et al.), pp. 132-152 (B. C. Decker Inc., Ontario, Canada, 2000).   |                |
| VB  | C5                       | Lyden, D. et al., Id1 and Id3 are required for neurogenesis, angiogenesis and vascularization of tumour xenografts, <i>Nature</i> , 401:670-677 (1999).   |                |
| VB  | C6                       | Streit, M. et al., Thrombospondin-2: a potent endogenous inhibitor of tumor growth and angiogenesis, <i>Proc Natl. Acad. Sci. USA</i> , 96:14888-14893 (1999).  |                |
| VB  | C7                       | Chin, L. et al., Essential role for oncogenic Ras in tumour maintenance, <i>Nature</i> , 400:468-472 (1999).  |                |
| ΫВ  | Taken MD and Author Club |   |                |
| VB Yao, Y. et al., Prognostic value of vascular endothelial growth factor   |                          | Yao, Y. et al., Prognostic value of vascular endothelial growth factor and its receptors Flt-1 and Flk-1 in astrocytic tumours, <i>Acta Neurochir (Wien)</i> , 143:159-66 (2001).   |                |
| VB  | C10                      | Yuan, A. et al., Aberrant p53 expression correlates with expression of vascular endothelial growth factor mRNA and interleukin-8 mRNA and neoangiogenesis in non-small-cell lung cancer, J. Clinical Oncology, 20:900-910 (2002). |                |

|            |  | - |
|------------|--|---|
| Examiner · | /v   |   |
| Signature  | /Venkataraman Balasubraman achsidered 10/02/2006 |   |
| - ig       | Considered                                       |   |

<sup>\*</sup>EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the Individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

<sup>&</sup>lt;sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

PTO/SB/08A/B 08-03) through 07/31/2006. OMB 0651-0031 J.S. DEPARTMENT OF COMMERCE Approved Patent and Trademark

To be assigned

701039-52585

Under the Paperwork Reduction Act of 199 persons are required to respond to a collection of information unle s it displays a valid OMB control number. Complete if Known Substitute for form 1449 PTO **Application Number** 10/511,009 INFORMATION DISCLOSURE Filing Date October 12, 2004 First Named Inventor Ronit Satchi-Fainaro et al. STATEMENT BY APPLICANT Art Unit To be assigned (use as many sheets as necessary)

Sheet

of

**Examiner Name** 

Attorney Docket Number

|      | т     |  |   |
|------|-------|--|---|
| . VI | B C11 | Ingber, D. et al., Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumour growth, <i>Nature</i> , 348:555-557 (1990).   | ٠ |
| VB   | C12   | Antoine, N. et al., AGM-1470, a potent angiogenesis inhibitor, prevents the entry of normal but not transformed endothelial cells into the G <sub>1</sub> phase of the cell cycle, Cancer Res., 54:2073-2076 (1994).                                 |   |
| VB   | C13   | Kudelka, A.P. et al., Complete remission of metastatic cervical cancer with the angiogenesis inhibitor TNP-470, N. Engl. J. Med., 338:991-2 (1998).  |   |
| VB   | C14   | Kudelka, A.P. et al., A phase I study of TNP-470 administered to patients with advanced squamous cell cancer of the cervix, Clinical Cancer Res., 3:1501-1505 (1997).  |   |
| VB   | C15   | Bhargava, P. et al., A Phase I and pharmacokinetic study of TNP-470 administered weekly to patients with advanced cancer, Clinical Cancer Res., 5:1989-1995 (1999).  |   |
| VB   | C16   | Herbst, R.S. et al., Safety and pharmacokinetic effects of TNP-470, an angiogenesis inhibitor, combined with paclitaxel in patients with solid tumors: evidence for activity in non-small-cell lung cancer, J. Clinical Oncol., 20:4440-4447 (2002). |   |
| VB   | C17   | Kim, E.S. et al., Angiogenesis inhibitors in lung cancer. Curr. Oncol. Rep., 4:325-333 (2002).   |   |
| . VB | C18   | Stadler, W.M. et al., Multi-institutional study of the angiogenesis inhibitor TNP-470 in metastatic renal carcinoma, J. Clinical Oncol., 17:2541-2545 (1999).  |   |
| VB   | C19   | Logothetis, C.J. et al., Phase I trial of the angiogenesis inhibitor TNP-470 for progressive androgen-independent prostate cancer. Clinical Cancer Res., 7:1198-1203 (2001).   |   |
| VB   | C20 . | Rupnick, M.A. et al., Adipose tissue mass can be regulated through the vasculature, <i>Proc. Natl. Acad. Sci. USA</i> , 99:10730-10735 (2002).   |   |
| VB   | C21   | Schoof, D.D. et al., The influence of angiogenesis inhibitor AGM-1470 on immune system status and tumor growth in vitro, <i>Int. J. Cancer</i> , 55:630-635 (1993).  |   |

| Examiner Signature /Venkataraman Balasubramanian Date Considered | 10/02/2006 |
|--|------------|
|--|------------|

<sup>\*</sup>EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

This collection of information is required by 37 CFR 1.98. The Information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450. If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Applicant's unique citation designation number (optional), <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

Approved to Patent and Trademark O

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number

Complete if Known Substitute for form 1449 PTO 10/511,009 **Application Number** INFORMATION DISCLOSURE October 12, 2004 **Filing Date** Ronit Satchi-Fainaro et al. First Named Inventor STATEMENT BY APPLICANT To be assigned Art Unit (use as many sheets as necessary) To be assigned **Examiner Name** 701039-52585 Sheet of **Attorney Docket Number** 

|    |       |  | - |
|----|-------|--|---|
| VB | C22   | Nagabuchi, E. et al., TNP-470 antiangiogenic therapy for advanced murine neuroblastoma,<br>J. Pediatric Surg., 32:287-93 (1997).   |   |
| VB | C23   | Rihova, B. et al., Biocompatibility of N-(2-hydroxypropyl) methacrylamide copolymers containing adnamycin. Immunogenicity, and effect on haematopoietic stem cells in bone marrow in vivo and mouse splenocytes and human peripheral blood lymphocytes in vitro, <i>Biomaterials</i> , 10:335-342. (1989). |   |
| VB | C24   | Seymour, L.W. et al., The pharmacokinetics of polymer-bound adriamycin, <i>Biochem. Pharmacol.</i> , 39:1125-1131 (1990).  |   |
| VE | C25   | Maeda, H. et al., Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review, J. Controlled Release, 65:271-284 (2000).   |   |
| VB | C26   | Duncan, R. et al., Preclinical toxicology of a novel polymeric antitumour agent: HPMA copolymer-doxorubicin (PK1), <i>Human and Exp. Toxicology</i> , 17:93-104 (1998).  |   |
| VB | C27   | Satchi-Fainaro, R., Targeting tumor vasculature: Reality or a dream?. J. Drug Targeting, 10:529-533 (2002).  |   |
| VE | C28   | Duncan, R. et al., Polymers containing enzymatically degradable bonds, 7. Design of oligopeptide side chains in poly [N-(2-hydroxypropyl)methacrylamide] copolymers to promote efficient degradation by lysosomal enzymes, Makromol. Chem., 184:1997-2008 (1983).  |   |
| VB | C29   | Foekens, J.A. et al., Prognostic significance of cathepsins B and L in primary human breast cancer. J. Clinical Oncol., 16:1013-1021 (1998).   |   |
| VB | C30 . | Gianasi, E. et al HPMA copolymer platinates as novel antitumour agents: in vitro properties, pharmacokinetics and antitumour activity in vivo, <i>Eur. J. Cancer</i> , 35:994-1002 (1999).   |   |
| VB | C31   | Kusaka, M. et al. Cytostatic inhibition of endothelial cell growth by the angiogenesis inhibitor TNP-470 (AGM-1470), Br. J. Cancer. 69:212-216 (1994).   |   |
| VB | C32   | Greene, A.K. et al., Endothelial-directed hepatic regeneration after partial hepatectomy,  Ann. Surg., 237:530-535 (2003)  |   |

| 1 |           |  |            |
|---|-----------|--|------------|
|   | Examiner  | /Venkataraman Balasubramania Date      | 40/00/0006 |
| 1 | Signature | /venkataraman Balasubramanian/psidered | 10/02/2006 |
|   | Signature |  | .,         |

<sup>\*</sup>EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English tanguage Translation is attached.

PTO/SB/08A/B 08-03) brough 07/31/2006. OMB 0651-0031 S. DEPARTMENT OF COMMERCE

Approved f Patent and Trademark O

Under the Paperwork Reduction Act of 1995, persons are required to respond to a collection of information unless it displays a valid OMB control number.

Complete If Known Substitute for form 1449 PTO 10/511,009 **Application Number** INFORMATION DISCLOSURE October 12, 2004 Filing Date Ronit Satchi-Fainaro et al. **First Named Inventor** STATEMENT BY APPLICANT Art Unit To be assigned (use as many sheets as necessary) To be assigned **Examiner Name** Sheet **Attorney Docket Number** 701039-52585

|         | 1   |   |   |
|---------|-----|---|---|
| VB<br>· | C33 | Drixler, T.A. et al., Liver regeneration is an angiogenesis- associated phenomenon, <i>Ann. Surg.</i> , 236:703-712 (2002).   |   |
| VB      | C34 | Klein, S.A. et al., Angiogenesis inhibitor TNP-470 inhibits murine cutaneous wound healing, <i>J. Surg. Res.</i> , 82:268-274 (1999).   | • |
| VB      | C35 | Whalen, C.T. et al., Assay of TNP-470 and its two major metabolites in human plasma by high-performance liquid chromatography-mass spectrometry, J. Chromatographic Sci., 40:214-218 (2002).  |   |
| VB      | C36 | Brocchini, S. et al., Polymer-Drug conjugates: drug release from pendent linkers. in<br>Encyclopaedia of controlled release (ed. Mathiovitz, E.) 786-816 (New York: Wiley, 1999).   |   |
| VB      | C37 | Duncan, R. et al., Polymer-drug conjugates, PDEPT and PELT: basic principles for design and transfer from the laboratory to clinic, J. Controlled Release, 74:135-146 (2001).   |   |
| VB      | C38 | Vasey, P.A. et al., Phase I clinical and pharmacokinetic study of PK1 [N-(2-hydroxypropyl)methacrylamide copolymer doxorubicin]: first member of a new class of chemotherapeutic agents-drug-polymer conjugates, Cancer Research Campaign Phase I/II Committee, Clinical Cancer Res., 5:83-94 (1999). |   |
| VB      | C39 | Seymour, L.W. et al., Tumour tropism and anti-cancer efficacy of polymer-based doxorubicin prodrugs in the treatment of subcutaneous murine B16F10 melanoma, Br. J. Cancer, 70:636-641 (1994).  |   |
| VB      | C40 | Dvorak, H.F. et al., Identification and characterization of the blood vessels of solid tumors that are leaky to circulating macromolecules. <i>Am. J. Pathology</i> , 133:95-109 (1988).  |   |
| VB      | C41 | Griffith, E.C. et al., Methionine aminopeptidase (type 2) is the common target for angiogenesis inhibitors AGM-1470 and ovalicin, <i>Chem. and Biol.</i> , 4, 461-471 (1997).   | • |
| · VB    | C42 | Auerbach, R. et al., Angiogenesis assays: problems and pitfalls, Cancer Metastasis Rev., 19:167-172 (2000).   |   |
| VB      | C43 | Seymour, L.W. et al., Hepatic drug targeting: phase I evaluation of polymer-bound doxorubicin., J. Clinical Oncol., 20:1668-1676 (2002).  |   |

| Examiner<br>Signature | /Venkataraman Balasubramanian Considered | 10/02/2006 |
|-----------------------|--|------------|

<sup>\*</sup>EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant."

This collection of Information is required by 37 CFR 1.98. The Information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

PTO/SB/08A/B 08-03) through 07/31/2006. OMB 0651-0031 D.S. DEPARTMENT OF COMMERCE Approved (
Patent and Trademark C

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

| Substitute for | Substitute for form 1449 PTO                    |        | · C                    | omplete if Known     |                             |
|----------------|---|--------|------------------------|----------------------|-----------------------------|
|                |   |        |                        | Application Number   | 10/511,009                  |
| INFO           | RMATIC  | N DISC | CLOSURE                | Filing Date          | October 12, 2004            |
| STA            | STATEMENT BY APPLICANT                          |        |                        | First Named Inventor | Ronit Satchi-Fainaro et al. |
| 0.2            |   |        |                        | Art Unit             | To be assigned              |
|                | (use as many sheets as necessary)  Sheet 6 of 6 |        | Examiner Name          | To be assigned       |                             |
| Sheet          |   |        | Attorney Docket Number | 701039-52585         |                             |

|      | Τ   |   | 1 |
|------|-----|---|---|
| VB   | C44 | Francis, G.E. et al., PEG-modified proteins. in Stability of Proteins Pharmaceuticals (Part B) (ed. Ahem TJ, M.M.) 235-263 (Plenum Press, New York, 1992).  |   |
| VB   | C45 | Ho, D.H. et al., Clinical pharmacology of polyethylene glycol-L-asparaginase, <i>Drug Metabolism Disposition</i> , 14:349-352 (1986).   |   |
| VB   | C46 | O'Reilly, M.S. et al., Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma, Cell, 79:315-328 (1994).                                      |   |
| VB   | C47 | Folkman, J. et al., Long-term culture of capillary endothelial cells, <i>Proc. Natl. Acad. Sci. USA</i> , 76:5217-5221 (1979).  |   |
| VB   | C48 | Waynforth, H.B. Routes and methods of administration, Intracerebral injection. in <i>Experimental and Surgical technique in the rat</i> , Vol. 2.9 34-36 (Academic Press, London, 1980).                | · |
| VB   | C49 | Bhargava, P. et al., A Phase I and pharmacokinetic study of TNP-470 administered weekly to patients with advanced cancer, Clinical Cancer Res., 5:1989-1995 (1999).                                     |   |
| VB   | C50 | Seymour, L.W. et al., The pharmacokinetics of polymer-bound adriamycin, <i>Biochemical Pharmacology</i> , 39:1125-1131 (1990).  |   |
| . VB | C51 | Yeh, J.R. et al., The antiangiogenic agent TNP-470 requires p53 and p21 <sup>CIP/WAF</sup> for endothelial cell growth arrest, <i>Proc. Natl. Acad. Sc. i USA</i> , 97:12782-12787 (2000).              |   |
| . VB | C52 | Zhang, Y. et al., Cell cycle inhibition by the anti-angiogenic agent TNP-470 is mediated by p53 and p21 WAFI/CIP1, Proc. Natl. Acad. Sci. USA, 97:6427-6432 (2000).                                     |   |
| VB   | C53 | Seymour, L.W. et al., N-(2-hydroxypropyl) methacrylamide copolymers targeted to the hepatocyte galactose-receptor: pharmacokinetics in DBA <sub>2</sub> mice, <i>Br. J. Cancer</i> , 63:859-866 (1991). |   |
| VB   | C54 | Folkman, J. Tumor angiogenesis. in <i>Accomplishments in cancer research</i> (eds. Wells, S.J. & Sharp, P.) 32-44 (Lippincott Williams & Wilkins, New York, 1998)                                       |   |

| Examiner<br>Signature | /Venkataraman BalasubramanianConsidered | 10/02/2006 |
|-----------------------|---|------------|

<sup>\*</sup>EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

<sup>1</sup> Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

PTO/SB/08A/B 08-03)

Approved for use through 07/31/2006, OMB 0651-0031
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

perwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Abstitute for form 1449 PTO

JUN 1 6 2005

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 1

|                        | Complete if Known    |   |
|------------------------|----------------------|---|
| Application Number     | 10/511,009           | _ |
| Filing Date            | 04/10/2003           |   |
| First Named Inventor   | Ronit Satchi-Fainaro |   |
| Art Unit               | To be assigned       |   |
| Examiner Name          | To be assigned       |   |
| Attorney Docket Number | 701039-052585-US     |   |

|                       |           |  | U.S. PATENT                    | DOCUMENTS  |  |
|-----------------------|-----------|--|--------------------------------|--|--|
| Examiner<br>Initials* | Cite No.1 | Document Number Number - Kind Code <sup>2</sup> (If known) | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines Where Relevant<br>Passages or Relevant<br>Figures Appear |
| AR                    | `A10      | 5.037.883  | 08/06/1991                     |  |  |
|                       | L         |  |                                | <del></del>  |  |

|                       | FOREIGN PATENT DOCUMENTS |   |                                |  |   |    |  |  |
|-----------------------|--------------------------|---|--------------------------------|--|---|----|--|--|
| Examiner<br>Initiats* | Cite No.1                | Foreign Patent Document  Country Code3 - Number4 - Kind Code5 (# known) | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant Of Cited Document | Pages, Columns, Lines<br>Where Relevant Passages<br>or Relevant Figures<br>Appear | t* |  |  |
|                       |                          |   |                                |  |   |    |  |  |

|                       | -         | NON PATENT LITERATURE DOCUMENTS  |              |  |  |  |  |
|-----------------------|-----------|--|--------------|--|--|--|--|
| Examiner<br>Initials* | Cite No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published |              |  |  |  |  |
|                       |           |  |              |  |  |  |  |
|                       |           |  | <del> </del> |  |  |  |  |
|                       |           |  |              |  |  |  |  |
|                       |           | )  |              |  |  |  |  |
|                       |           |  | _            |  |  |  |  |
|                       |           | ·  |              |  |  |  |  |
|                       |           |  |              |  |  |  |  |
|                       |           |  |              |  |  |  |  |

| -                     |  |            |
|-----------------------|--|------------|
| Examiner<br>Signature | /Venkataraman BalasubramanianPate Considered | 10/02/2006 |

<sup>\*</sup>EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

This collection of Information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

<sup>1</sup> Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

PTO/SB/08A/B 08-03)
Approved for use through 07/31/2006, OMB 0651-0031
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.



| Substitute for                          | ubstitute for form 1449 PTO       |        |         |                        | Complete if Known    |
|---|-----------------------------------|--------|---------|------------------------|----------------------|
|   |                                   |        |         | Application Number     | 10/511,009           |
| INFO                                    | RMATIC                            | ON DIS | CLOSURE | Filing Date            | 04/10/2003           |
| STAT                                    | STATEMENT BY APPLICANT            |        |         | First Named Inventor   | Ronit Satchi-Fainaro |
| • |                                   |        |         | Art Unit               | To be assigned       |
|   | (use as many sheets as necessary) |        |         | Examiner Name          | To be assigned       |
| Sheet                                   | 1                                 | of     | 1       | Attorney Docket Number | 701039-052585-US     |

|                    | U.S. PATENT DOCUMENTS |   |                                |  |  |  |  |
|--------------------|-----------------------|---|--------------------------------|--|--|--|--|
| Examiner tritials* | Cite No.1             | Document Number  Number – Kind Code <sup>a</sup> (ii known) | Publication Date<br>MM-0D-YYYY | Name of Patentes or<br>Applicant of Cited Document | Pages, Columns, Lines Where Relevant<br>Passages or Relevant<br>Figures Appear |  |  |
|                    |                       |   |                                |  |  |  |  |
|                    |                       |   |                                |  |  |  |  |

|                    |  | FOR  | EIGN PATENT I       | OCUMENTS                                   |   |                |
|--------------------|--|--|---------------------|--|---|----------------|
| Examiner Cite No.1 | Foreign Patent Document                        | Publication Date                               | Name of Patentee or | Pages, Columns,<br>Lines<br>Where Relevant |   |                |
|                    | Country Code3 - Number4 - Kind Co<br>(# known) | Country Code3 - Number4 - Kind Code5 (# known) | MM-DD-YYYY          | Applicant Of Cited Document                | Passages<br>or Relevant Figures<br>Appaar | T <sup>a</sup> |
| VB                 | B2   | WO 01/36002                                    | 05/25/01            | SEARLE FRANCES et al.                      |   |                |
| VB                 | В3   | WO 02/098446                                   | 12/12/02            | EKWURIBE NNOCHIRI et al.                   |   |                |

|                       | NON PATENT LITERATURE DOCUMENTS |  |    |  |  |
|-----------------------|---------------------------------|--|----|--|--|
| Examiner<br>Initials* | Cite No.1                       | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T² |  |  |
| VB                    | C55                             | NOGUCHI, A., et al., <i>Bioconjugate Chem., 3 (2):</i> 132-137 (1992).   |    |  |  |
| VB                    | C56                             | YASUKAWA, T., et al., <i>IOVS 40 (11)</i> : 2690-2696 (1999).  |    |  |  |
| VВ                    | C57                             | YAMAOKA, T., et al, Journal of Pharmaceutical Sciences, 83 (4): 601-606 (1994).  |    |  |  |
| VB                    | C58                             | YAMAOKA, T., et al., Journal of Pharmaceutical Pharmacology, 47: 479-486 (1995).   |    |  |  |
| VB                    | C59                             | MURAKAMI, Y., et al., <i>Drug Delivery, 4</i> : 23-31 (1997).  |    |  |  |

| Examiner<br>Signature | /Venkataraman | Balasubramanian Pat | e<br>sidered | 10/02/2006 |
|-----------------------|---------------|---------------------|--------------|------------|
| Oignature             |               |                     | Sidered      |            |

<sup>\*</sup>EXAMINER if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

This collection of information is required by 37 CFR 1.98. The Information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450. If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

<sup>1</sup> Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

PTO/SB/08A/B 08-03)

Approved for use through 07/31/2006. OMB 0651-0031 Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE eperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Substitute for form 1449 PTO

TRADE

## **INFORMATION DISCLOSURE** STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet of

| COMPLETE IF KNOWN      |                      |   |  |  |
|------------------------|----------------------|---|--|--|
| Application Number     | 10/511,009           | - |  |  |
| Filing Date            | 04/10/2003           | - |  |  |
| First Named Inventor   | Ronit Satchi-Fainaro | • |  |  |
| Art Unit               | 1624                 | • |  |  |
| Examiner Name          | B. Bala              | - |  |  |
| Attorney Docket Number | 701039-052585-US     |   |  |  |

|                      | U.S. PATENT DOCUMENTS |   |                  |  |  |  |
|----------------------|-----------------------|---|------------------|--|--|--|
| xaminer<br>Initials* | Cite No. <sup>1</sup> | Number - Kind Code <sup>2</sup> (# known) | Publication Date | Name of Patentee or<br>Applicant of Cried Document | Pages, Columns, Lines Where Relevant<br>Passages or Relevant<br>Figures Appear |  |
|                      |                       |   |                  |  |  |  |

|                       | <u>F</u> (   | OREIGN PATENT DO  | <u>DCUMENTS</u>                |  |   |    |
|-----------------------|--------------|---|--------------------------------|--|---|----|
| Examiner<br>Initials* | Cite<br>No.1 | Foreign Patent Document  Country Code3 - Number4 - Kind Code5 (# known) | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant Of Cited Document | Pages, Columns,<br>Lines<br>Where Ralevant<br>Passages<br>or Relevant Figures<br>Appear | T* |
| VB                    | B4           | WO 03/086178 A  | 10/23/2003                     |  | ·   |    |

|                       | NO           | ON PATENT LITERATURE DOCUMENTS   |    |
|-----------------------|--------------|--|----|
| Examiner<br>Initials* | Cite<br>No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | τ² |
| VB                    | C60          | Satchi, R. et al., <i>British J. of Cancer</i> , 85(7):1070-1076 (2001).   |    |
|                       |              |  |    |

| Examiner<br>Signature | /Venkataraman Balasubramanian Considered | 10/02/2006 |
|-----------------------|--|------------|
| Signature             | Considered                               |            |

<sup>\*</sup>EXAMINER If reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450. If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.